

Val Ala Thr Asp Ala

1

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## SEQUENCE LISTING

<110> Anthony Rosen Donald W. Nicholson Livia Casciola-Rosen Felipe A. Andrade Sophie Roy Nancy A. Thornberry <120> AUTOANTIGENIC FRAGMENTS, METHODS AND **ASSAYS** <130> 20221Y <140> 09/296,662 <141> 1999-04-22 <150> PCT/US99/08774 <151> 1999-04-22 <150> 60/000,060 <151> 1998-04-22 <160> 37 <170> FastSEQ for Windows Version 4.0 <210> 1 <211> 4 <212> PRT <213> Human <400> 1 Asp Glu Val Asp <210> 2 <211> 4 <212> PRT <213> Human <400> 2 Ile Glu Ala Asp <210> 3 <211> 5 <212> PRT <213> Human <400> 3

**RECEIVED** 

APR 1 6 2003

TECH CENTER 1600/2900

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Lys Lys Ala His Gly Leu Leu Ala Glu Glu Asn Arg Gly Leu Gly Glu Arg Ala Asn Leu Gly Arg Gln Phe Leu Glu Val Glu Leu Asp Gln Ala Arg Glu Lys Tyr Val Gln Glu Leu Ala Ala Val Arg Ala Asp Ala Glu Thr Arg Leu Ala Glu Val Gln Arg Glu Ala Gln Ser Thr Ala Arg Glu Leu Glu Val Met Thr Ala Lys Tyr Glu Gly Ala Lys Val Lys Val Leu Glu Glu Arg Gln Arg Phe Gln Glu Glu Arg Gln Lys Leu Thr Ala Gln Val Glu Glu Leu Ser Lys Lys Leu Ala Asp Ser Asp Gln Ala Ser Lys Val Gln Gln Gln Lys Leu Lys Ala Val Gln Ala Gln Gly Gly Glu Ser Gln Gln Glu Ala Gln Arg Phe Gln Ala Gln Leu Asn Glu Leu Gln Ala Gln Leu Ser Gln Lys Glu Gln Ala Ala Glu His Tyr Lys Leu Gln Met Glu Lys Ala Lys Thr His Tyr Asp Ala Lys Lys Gln Gln Asn Gln Glu Leu Gln Glu Gln Leu Arg Ser Leu Glu Gln Leu Gln Lys Glu Asn Lys Glu Leu Arg Ala Glu Ala Glu Arg Leu Gly His Glu Leu Gln Gln Ala Gly Leu Lys Thr Lys Glu Ala Glu Gln Thr Cys Arg His Leu Thr Ala Gln Val Arg Ser Leu Glu Ala Gln Val Ala His Ala Asp Gln Gln Leu Arg Asp Leu Gly Lys Phe Gln Val Ala Thr Asp Ala Leu Lys Ser Arg Glu Pro Gln Ala Lys Pro Gln Leu Asp Leu Ser Ile Asp Ser Leu Asp Leu Ser Cys Glu Glu Gly Thr Pro Leu Ser Ile Thr Ser Lys Leu Pro Arg Thr Gln Pro Asp Gly Thr Ser Val Pro Gly Glu Pro Ala Ser Pro Ile Ser Gln Arg Leu Pro Pro Lys Val Glu Ser Leu Glu Ser Leu Tyr Phe Thr Pro Ile Pro Ala Arg Ser Gln Ala Pro Leu Glu Ser Ser Leu Asp Ser Leu Gly Asp Val Phe Leu Asp Ser Gly Arg Lys Thr Arg Ser Ala Arg Arg Arg Thr Thr Gln Ile Ile Asn Ile Thr Met Thr Lys Lys Leu Asp Val Glu Glu Pro Asp Ser Ala Asn Ser Ser Phe Tyr Ser Thr Arg Ser Ala Pro Ala Ser Gln Ala Ser Leu Arg Ala Thr Ser Ser Thr Gln Ser Leu Ala Arg Leu Gly Ser Pro Asp Tyr Gly Asn Ser Ala Leu Leu Ser Leu Pro Gly Tyr Arg Pro Thr Thr Arg Ser Ser Ala Arg Arg 

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Glu Asp Leu Glu Asn Phe Leu Gln Lys Ala Pro Val Pro Ser Thr Cys Ser Ser Thr Phe Pro Glu Glu Leu Ser Pro Pro Ser His Gln Ala Lys Arg Glu Ile Arg Phe Leu Glu Leu Gln Lys Val Ala Ser Ser Ser Ser Gly Asn Asn Phe Leu Ser Gly Ser Pro Ala Ser Pro Met Gly Asp Ile Leu Gln Thr Pro Gln Phe Gln Met Arg Arg Leu Lys Lys Gln Leu Ala Asp Glu Arg Ser Asn Arg Asp Glu Leu Glu Leu Glu Leu Ala Glu Asn Arg Lys Leu Leu Thr Glu Lys Asp Ala Gln Ile Ala Met Met Gln Gln Arg Ile Asp Arg Leu Ala Leu Leu Asn Glu Lys Gln Ala Ala Ser Pro Leu Glu Pro Lys Glu Leu Glu Glu Leu Arg Asp Lys Asn Glu Ser Leu Thr Met Arg Leu His Glu Thr Leu Lys Gln Cys Gln Asp Leu Lys Thr Glu Lys Ser Gln Met Asp Arg Lys Ile Asn Gln Leu Ser Glu Glu Asn Gly Asp Leu Ser Phe Lys Leu Arg Glu Phe Ala Ser His Leu Gln Gln Leu Gln Asp Ala Leu Asn Glu Leu Thr Glu Glu His Ser Lys Ala Thr Gln Glu Trp Leu Glu Lys Gln Ala Gln Leu Glu Lys Glu Leu Ser Ala Ala Leu Gln Asp Lys Lys Cys Leu Glu Glu Lys Asn Glu Ile Leu Gln Gly Lys Leu Ser Gln Leu Glu Glu His Leu Ser Gln Leu Gln Asp Asn Pro Pro Gln Glu Lys Gly Glu Val Leu Gly Asp Val Leu Gln Leu Glu Thr Leu Lys Gln Glu Ala Ala Thr Leu Ala Ala Asn Asn Thr Gln Leu Gln Ala Arg Val Glu Met Leu Glu Thr Glu Arg Gly Gln Gln Glu Ala Lys Leu Leu Ala Glu Arg Gly His Phe Glu Glu Glu Lys Gln Gln Leu Ser Ser Leu Ile Thr Asp Leu Gln Ser Ser Ile Ser Asn Leu Ser Gln Ala Lys Glu Glu Leu Glu Gln Ala Ser Gln Ala His Gly Ala Arg Leu Thr Ala Gln Val Ala Ser Leu Thr Ser Glu Leu Thr Thr Leu Asn Ala Thr Ile Gln Gln Gln Asp Gln Glu Leu Ala Gly Leu Lys Gln Gln Ala Lys Glu Lys Gln Ala Gln Leu Ala Gln Thr Leu Gln Gln Gln Glu Gln Ala Ser Gln Gly Leu Arg His Gln Val Glu Gln Leu Ser Ser Leu Lys Gln Lys Glu Gln Leu Lys Glu Val Ala Glu Lys Gln Glu Ala 

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Lys Lys Ala His Gly Leu Leu Ala Glu Glu Asn Arg Gly Leu Gly Glu Arg Ala Asn Leu Gly Arg Gln Phe Leu Glu Val Glu Leu Asp Gln Ala Arg Glu Lys Tyr Val Gln Glu Leu Ala Ala Val Arg Ala Asp Ala Glu Thr Arg Leu Ala Glu Val Gln Arg Glu Ala Gln Ser Thr Ala Arg Glu Leu Glu Val Met Thr Ala Lys Tyr Glu Gly Ala Lys Val Lys Val Leu Glu Glu Arg Gln Arg Phe Gln Glu Glu Arg Gln Lys Leu Thr Ala Gln Val Glu Gln Leu Glu Val Phe Gln Arg Glu Gln Thr Lys Gln Val Glu Glu Leu Ser Lys Lys Leu Ala Asp Ser Asp Gln Ala Ser Lys Val Gln Gln Gln Lys Leu Lys Ala Val Gln Ala Gln Gly Gly Glu Ser Gln Gln Glu Ala Gln Arg Leu Gln Ala Gln Leu Asn Glu Leu Gln Ala Gln Leu Ser Gln Lys Glu Gln Ala Ala Glu His Tyr Lys Leu Gln Met Glu Lys Ala Lys Thr His Tyr Asp Ala Lys Lys Gln Gln Asn Gln Glu Leu Gln Glu Gln Leu Arg Ser Leu Glu Gln Leu Gln Lys Glu Asn Lys Glu Leu Arg Ala Glu Ala Glu Arg Leu Gly His Glu Leu Gln Gln Ala Gly Leu Lys Thr Lys Glu Ala Glu Gln Thr Cys Arg His Leu Thr Ala Gln Val Arg Ser Leu Glu Ala Gln Val Ala His Ala Asp Gln Gln Leu Arg Asp Leu Gly Lys Phe Gln Val Ala Thr Asp Ala Leu Lys Ser Arg Glu Pro Gln Ala Lys Pro Gln Leu Asp Leu Ser Ile Asp Ser Leu Asp Leu Ser Cys Glu Glu Gly Thr Pro Leu Ser Ile Thr Ser Lys Leu Pro Arg Thr Gln Pro Asp Gly Thr Ser Val Pro Gly Glu Pro Ala Ser Pro Ile Ser Gln Arg Leu Pro Pro Lys Val Glu Ser Leu Glu Ser Leu Tyr Phe Thr Pro Ile Pro Ala Arg Ser Gln Ala Pro Leu Glu Ser Ser Leu Asp Ser Leu Gly Asp Val Phe Gln Asp Ser Gly Arg Lys Thr Arg Ser Ala Arg Arg Arg Thr Thr Gln Ile Ile Asn Ile Thr Met Thr Lys Lys Leu Asp Val Glu Glu Pro Asp Ser Ala Asn Ser Ser Phe Tyr Ser Thr Arg Ser Ala Pro Ala Ser Gln Ala Ser Leu Arg Ala Thr Ser Ser Thr Gln Ser Leu Ala Arg Leu Gly Ser Pro Asp Tyr Gly Asn Ser Ala Leu Leu Ser 



Leu Pro Gly Tyr Arg Pro Thr Thr Arg Ser Ser Ala Arg Arg Ser Gln 1875 1880 1885 Ala Gly Val Ser Ser Gly Ala Pro Pro Gly Arg Asn Ser Phe Tyr Met 1895 1900 Gly Thr Cys Gln Asp Glu Pro Glu Gln Leu Asp Asp Trp Asn Arg Ile 1910 1915 Ala Glu Leu Gln Gln Arg Asn Arg Val Cys Pro Pro His Leu Lys Thr 1925 1930 Cys Tyr Pro Leu Glu Ser Arg Pro Ser Leu Ser Leu Gly Thr Ile Thr 1940 1945 Asp Glu Glu Met Lys Thr Gly Asp Pro Gln Glu Thr Leu Arg Arg Ala 1955 1960 1965 Ser Met Gln Pro Ile Gln Ile Ala Glu Gly Thr Gly Ile Thr Thr Arg 1975 1980 Gln Gln Arg Lys Arg Val Ser Leu Glu Pro His Gln Gly Pro Gly Thr 1990 1995 Pro Glu Ser Lys Lys Ala Thr Ser Cys Phe Pro Arg Pro Met Thr Pro 2005 2010 Arg Asp Arg His Glu Gly Arg Lys Gln Ser Thr Thr Glu Ala Gln Lys 2025 Lys Ala Ala Pro Ala Ser Thr Lys Gln Ala Asp Arg Arg Gln Ser Met 2040 2045 Ala Phe Ser Ile Leu Asn Thr Pro Lys Lys Leu Gly Asn Ser Leu Leu 2055 2060 Arg Arg Gly Ala Ser Lys Lys Ala Leu Ser Lys Ala Ser Pro Asn Thr 2070 2075 Arg Ser Gly Thr Arg Arg Ser Pro Arg Ile Ala Thr Thr Ala Ser 2085 2090 Ala Ala Thr Ala Ala Ala Ile Gly Ala Thr Pro Arg Ala Lys Gly Lys 2105 Ala Lys His 2115 <210> 34 <211> 4096 <212> PRT <213> Human <220> <221> VARIANT <222> (1)...(4096) <223> Xaa = Any Amino Acid <400> 34 Met Ala Gly Ser Gly Ala Gly Val Arg Cys Ser Leu Leu Arg Leu Gln 10 Glu Thr Leu Ser Ala Ala Asp Arg Cys Gly Ala Ala Leu Ala Gly His 25 Gln Leu Ile Arg Gly Leu Gly Gln Glu Cys Val Leu Ser Ser Pro 40 Ala Val Leu Ala Leu Gln Thr Ser Leu Val Phe Ser Arg Asp Phe Gly 55 60 Leu Leu Val Phe Val Arg Lys Ser Leu Asn Ser Ile Glu Phe Arg Glu

75

Cys Arg Glu Glu Ile Leu Lys Phe Leu Cys Ile Phe Leu Glu Lys Met Gly Gln Lys Ile Ala Pro Tyr Ser Val Glu Ile Lys Asn Thr Cys Thr 105 Ser Val Tyr Thr Lys Asp Arg Ala Ala Lys Cys Lys Ile Pro Ala Leu 120 Asp Leu Leu Ile Lys Leu Leu Gln Thr Phe Arg Ser Ser Arg Leu Met 135 140 Asp Glu Phe Lys Ile Gly Glu Leu Phe Ser Lys Phe Tyr Gly Glu Leu 150 155 Ala Leu Lys Lys Ile Pro Asp Thr Val Leu Glu Lys Val Tyr Glu 165 170 Leu Leu Gly Leu Leu Gly Glu Val His Pro Ser Glu Met Ile Asn Asn 180 185 Ala Glu Asn Leu Phe Arg Ala Phe Leu Gly Glu Leu Lys Thr Gln Met 200 Thr Ser Ala Val Arg Glu Pro Lys Leu Pro Val Leu Ala Gly Cys Leu 215 Lys Gly Leu Ser Ser Leu Leu Cys Asn Phe Thr Lys Ser Met Glu Glu 235 Asp Pro Gln Thr Ser Arg Glu Ile Phe Asn Phe Val Leu Lys Ala Ile 250 Arg Pro Gln Ile Asp Leu Lys Arg Tyr Ala Val Pro Ser Ala Gly Leu 265 Arg Leu Phe Ala Leu His Ala Ser Gln Phe Ser Thr Cys Leu Leu Asp 280 Asn Tyr Val Ser Leu Phe Glu Val Leu Ile Lys Trp Cys Ala His Thr 295 300 Asn Val Glu Leu Lys Lys Ala Ala Leu Ser Ala Leu Glu Ser Phe Leu 310 315 Lys Gln Val Ser Asn Met Val Ala Lys Asn Ala Glu Met His Lys Asn Lys Leu Gln Tyr Glu Met Glu Gln Phe Tyr Gly Ile Ile Arg Asn Val 345 Asp Ser Asn Asn Lys Glu Leu Ser Ile Ala Ile Arg Gly Tyr Gly Leu 360 Phe Ala Gly Pro Cys Lys Val Ile Asn Ala Lys Asp Val Asp Phe Met 375 380 Tyr Val Glu Leu Ile Gln Arg Cys Lys Gln Met Phe Leu Thr Gln Thr 390 395 Asp Thr Gly Asp Tyr Arg Val Tyr Gln Met Pro Ser Phe Leu Gln Ser 405 410 Val Ala Ser Val Leu Leu Tyr Leu Asp Thr Val Pro Glu Val Tyr Thr 425 Pro Val Leu Glu His Leu Val Val Met Gln Ile Asp Ser Phe Pro Gln 440 Tyr Ser Pro Lys Met Gln Leu Val Cys Cys Arg Ala Ile Val Lys Val 455 Phe Leu Ala Leu Ala Ala Lys Gly Pro Val Leu Arg Asn Cys Ile Ser 470 475 Thr Val Val His Gln Gly Leu Ile Arg Ile Cys Ser Lys Pro Val Val 485 490 Leu Pro Lys Gly Pro Glu Ser Glu Ser Glu Asp His Arg Ala Ser Gly 505



Glu Val Arg Thr Gly Lys Trp Lys Val Pro Thr Tyr Lys Asp Tyr Val 520 525 Asp Leu Phe Arg His Leu Leu Ser Ser Asp Gln Met Met Asp Ser Ile 535 540 Leu Ala Asp Glu Ala Phe Phe Ser Val Asn Ser Ser Ser Glu Ser Leu 550 555 Asn His Leu Leu Tyr Asp Glu Phe Val Lys Ser Val Leu Lys Ile Val 565 570 Glu Lys Leu Asp Leu Thr Leu Glu Ile Gln Thr Val Gly Glu Gln Glu 585 Asn Gly Asp Glu Ala Pro Gly Val Trp Met Ile Pro Thr Ser Asp Pro 600 Ala Ala Asn Leu His Pro Ala Lys Pro Lys Asp Phe Ser Ala Phe Ile 615 Asn Leu Val Glu Phe Cys Arg Glu Ile Leu Pro Glu Lys Gln Ala Glu 630 Phe Phe Glu Pro Trp Val Tyr Ser Phe Ser Tyr Glu Leu Ile Leu Gln 650 Ser Thr Arg Leu Pro Leu Ile Ser Gly Phe Tyr Lys Leu Leu Ser Ile 665 Thr Val Arg Asn Ala Lys Lys Ile Lys Tyr Phe Glu Gly Val Ser Pro 680 Lys Ser Leu Lys His Ser Pro Glu Asp Pro Glu Lys Tyr Ser Cys Phe 695 700 Ala Leu Phe Val Lys Phe Gly Lys Glu Val Ala Val Lys Met Lys Gln 710 715 Tyr Lys Asp Glu Leu Leu Ala Ser Cys Leu Thr Phe Leu Leu Ser Leu 725 730 Pro His Asn Ile Ile Glu Leu Asp Val Arg Ala Tyr Val Pro Ala Leu 745 Gln Met Ala Phe Lys Leu Gly Leu Ser Tyr Thr Pro Leu Ala Glu Val 760 Gly Leu Asn Ala Leu Glu Glu Trp Ser Ile Tyr Ile Asp Arg His Val 775 780 Met Gln Pro Tyr Tyr Lys Asp Ile Leu Pro Cys Leu Asp Gly Tyr Leu 790 795 Lys Thr Ser Ala Leu Ser Asp Glu Thr Lys Asn Asn Trp Glu Val Ser 805 810 Ala Leu Ser Arg Ala Ala Gln Lys Gly Phe Asn Lys Val Val Leu Lys 820 825 His Leu Lys Lys Thr Lys Asn Leu Ser Ser Asn Glu Ala Ile Ser Leu 840 Glu Glu Ile Arg Ile Arg Val Val Gln Met Leu Gly Ser Leu Gly Gly 855 860 Gln Ile Asn Lys Asn Leu Leu Thr Val Thr Ser Ser Asp Glu Met Met 870 875 Lys Ser Tyr Val Ala Trp Asp Arg Glu Lys Arg Leu Ser Phe Ala Val 885 890 Pro Phe Arg Glu Met Lys Pro Val Ile Phe Leu Asp Val Phe Leu Pro 900 905 Arg Val Thr Glu Leu Ala Leu Thr Ala Ser Asp Arg Gln Thr Lys Val 920 925 Ala Ala Cys Glu Leu Leu His Ser Met Val Met Phe Met Leu Gly Lys 935



Ala Thr Gln Met Pro Glu Gly Gly Gln Gly Ala Pro Pro Met Tyr Gln Leu Tyr Lys Arg Thr Phe Pro Val Leu Leu Arg Leu Ala Cys Asp Val Asp Gln Val Thr Arg Gln Leu Tyr Glu Pro Leu Val Met Gln Leu Ile His Trp Phe Thr Asn Asn Lys Lys Phe Glu Ser Gln Asp Thr Val Ser Leu Leu Glu Ala Ile Leu Asp Gly Ile Val Asp Pro Val Asp Ser Thr Leu Arg Asp Phe Cys Gly Arg Cys Ile Arg Glu Phe Leu Lys Trp Ser Ile Lys Gln Ile Thr Pro Gln Gln Gln Glu Lys Ser Pro Val Asn Thr Lys Ser Leu Phe Lys Arg Leu Tyr Ser Leu Ala Leu His Pro Asn Ala Phe Lys Arg Leu Gly Ala Ser Leu Ala Phe Asn Asn Ile Tyr Arg Glu Phe Arg Glu Glu Ser Leu Val Glu Gln Phe Val Phe Glu Ala Leu Val Ile Tyr Met Glu Ser Leu Ala Leu Ala His Ala Asp Glu Lys Ser Leu Gly Thr Ile Gln Gln Cys Cys Asp Ala Ile Asp His Leu Cys Arg Ile Ile Glu Lys Lys His Val Ser Leu Asn Lys Ala Lys Lys Arg Arg Leu Pro Arg Gly Phe Pro Pro Ser Ala Ser Leu Cys Leu Leu Asp Leu Val Lys Trp Leu Leu Ala His Cys Gly Arg Pro Gln Thr Glu Cys Arg His Lys Ser Ile Glu Leu Phe Tyr Lys Phe Val Pro Leu Leu Pro Gly Asn Arg Ser Pro Asn Leu Trp Leu Lys Asp Val Leu Lys Glu Gly Val Ser Phe Leu Ile Asn Thr Phe Glu Gly Gly Gly Cys Gly Gln Pro Ser Gly Ile Leu Ala Gln Pro Thr Leu Leu Tyr Leu Arg Gly Pro Phe Ser Leu Gln Ala Thr Leu Cys Trp Leu Asp Leu Leu Leu Ala Ala Leu Glu Cys Tyr Asn Thr Phe Ile Gly Glu Arg Thr Val Gly Ala Leu Gln Val Leu Gly Thr Glu Ala Gln Ser Ser Leu Leu Lys Ala Val Ala Phe Phe Leu Glu Ser Ile Ala Met His Asp Ile Ile Ala Ala Glu Lys Cys Phe Gly Thr Gly Ala Ala Gly Asn Arg Thr Ser Pro Gln Glu Gly Glu Arg Tyr Asn Tyr Ser Lys Cys Thr Val Val Val Arg Ile Met Glu Phe Thr Thr Thr Leu Leu Asn Thr Ser Pro Glu Gly Trp Lys Leu Leu Lys Lys Asp Leu Cys Asn Thr His Leu Met Arg Val Leu Val Gln Thr Leu 



Cys Glu Pro Ala Ser Ile Gly Phe Asn Ile Gly Asp Val Gln Val Met Ala His Leu Pro Asp Val Cys Val Asn Leu Met Lys Ala Leu Lys Met Ser Pro Tyr Lys Asp Ile Leu Glu Thr His Leu Arg Glu Lys Ile Thr Ala Gln Ser Ile Glu Glu Leu Cys Ala Val Asn Leu Tyr Gly Pro Asp Ala Gln Val Asp Arg Ser Arg Leu Ala Ala Val Val Ser Ala Cys Lys Gln Leu His Arg Ala Gly Leu Leu His Asn Ile Leu Pro Ser Gln Ser Thr Asp Leu His His Ser Val Gly Thr Glu Leu Leu Ser Leu Val Tyr Lys Gly Ile Ala Pro Gly Asp Glu Arg Gln Cys Leu Pro Ser Leu Asp Leu Ser Cys Lys Gln Leu Ala Ser Gly Leu Leu Glu Leu Ala Phe Ala Phe Gly Gly Leu Cys Glu Arg Leu Val Ser Leu Leu Leu Asn Pro Ala Val Leu Ser Thr Ala Ser Leu Gly Ser Ser Gln Gly Ser Val Ile His Phe Ser His Gly Glu Tyr Phe Tyr Ser Leu Phe Ser Glu Thr Ile Asn Thr Glu Leu Leu Lys Asn Leu Asp Leu Ala Val Leu Glu Leu Met Gln Ser Ser Val Asp Asn Thr Lys Met Val Ser Ala Val Leu Asn Gly Met Leu Asp Gln Ser Phe Arg Glu Arg Ala Asn Gln Lys His Gln Gly Leu Lys Leu Ala Thr Thr Ile Leu Gln His Trp Lys Lys Cys Asp Ser Trp Trp Ala Lys Asp Ser Pro Leu Glu Thr Lys Met Ala Val Leu Ala Leu Leu Ala Lys Ile Leu Gln Ile Asp Ser Ser Val Ser Phe Asn Thr Ser His Gly Ser Phe Pro Glu Val Phe Thr Thr Tyr Ile Ser Leu Leu Ala Asp Thr Lys Leu Asp Leu His Leu Lys Gly Gln Ala Val Thr Leu Leu Pro Phe Phe Thr Ser Leu Thr Gly Gly Ser Leu Glu Glu Leu Arg Arg Val Leu Glu Gln Leu Ile Val Ala His Phe Pro Met Gln Ser Arg Glu Phe Pro Pro Gly Thr Pro Arg Phe Asn Asn Tyr Val Asp Cys Met Lys Lys Phe Leu Asp Ala Leu Glu Leu Ser Gln Ser Pro Met Leu Leu Glu Leu Met Thr Glu Val Leu Cys Arg Glu Gln Gln His Val Met Glu Glu Leu Phe Gln Ser Ser Phe Arg Arg Ile Ala Arg Arg Gly Ser Cys Val Thr Gln Val Gly Leu Leu Glu Ser Val Tyr Glu Met Phe Arg Lys Asp 

FI

Asp Pro Arg Leu Ser Phe Thr Arg Gln Ser Phe Val Asp Arg Ser Leu Leu Thr Leu Leu Trp His Cys Ser Leu Asp Ala Leu Arg Glu Phe Phe Ser Thr Ile Val Val Asp Ala Ile Asp Val Leu Lys Ser Arg Phe Thr Lys Leu Asn Glu Ser Thr Phe Asp Thr Gln Ile Thr Lys Lys Met Gly Tyr Tyr Lys Ile Leu Asp Val Met Tyr Ser Arg Leu Pro Lys Asp Asp Val His Ala Lys Glu Ser Lys Ile Asn Gln Val Phe His Gly Ser Cys Ile Thr Glu Gly Asn Glu Leu Thr Lys Thr Leu Ile Lys Leu Cys Tyr Asp Ala Phe Thr Glu Asn Met Ala Gly Glu Asn Gln Leu Leu Glu Arg Arg Arg Leu Tyr His Cys Ala Ala Tyr Asn Cys Ala Ile Ser Val Ile Cys Cys Val Phe Asn Glu Leu Lys Phe Tyr Gln Gly Phe Leu Phe Ser Glu Lys Pro Glu Lys Asn Leu Leu Ile Phe Glu Asn Leu Ile Asp Leu Lys Arg Arg Tyr Asn Phe Pro Val Glu Val Glu Val Pro Met Glu Arg Lys Lys Lys Tyr Ile Glu Ile Arg Lys Glu Ala Arg Glu Ala Ala Asn Gly Asp Ser Asp Gly Pro Ser Tyr Met Ser Ser Leu Ser Tyr Leu Ala Asp Ser Thr Leu Ser Glu Glu Met Ser Gln Phe Asp Phe Ser Thr Gly Val Gln Ser Tyr Ser Tyr Ser Ser Gln Asp Pro Arg Pro Ala Thr Gly Arg Phe Arg Arg Glu Gln Arg Asp Pro Thr Val His Asp Asp Val Leu Glu Leu Glu Met Asp Glu Leu Asn Arg His Glu Cys Met Ala Pro Leu Thr Ala Leu Val Lys His Met His Arg Ser Leu Gly Pro Pro Gln Gly Glu Glu Asp Ser Val Pro Arg Asp Leu Pro Ser Trp Met Lys Phe Leu His Gly Lys Leu Gly Asn Pro Ile Val Pro Leu Asn Ile Arg Leu Phe Leu Ala Lys Leu Val Ile Asn Thr Glu Glu Val Phe Arg Pro Tyr Ala Lys His Trp Leu Ser Pro Leu Leu Gln Leu Ala Ala Ser Glu Asn Asn Gly Gly Glu Gly Ile His Tyr Met Val Val Glu Ile Val Ala Thr Ile Leu Ser Trp Thr Gly Leu Ala Thr Pro Thr Gly Val Pro Lys Asp Glu Val Leu Ala Asn Arg Leu Leu Asn Phe Leu Met Lys His Val Phe His Pro Lys Arg Ala Val Phe Arg His Asn Leu Glu Ile Ile Lys Thr 



Leu Val Glu Cys Trp Lys Asp Cys Leu Ser Ile Pro Tyr Arg Leu Ile Phe Glu Lys Phe Ser Gly Lys Asp Pro Asn Ser Lys Asp Asn Ser Val Gly Ile Gln Leu Leu Gly Ile Val Met Ala Asn Asp Leu Pro Pro Tyr Asp Pro Gln Cys Gly Ile Gln Ser Ser Glu Tyr Phe Gln Ala Leu Val Asn Asn Met Ser Phe Val Arg Tyr Lys Glu Val Tyr Ala Ala Ala Ala Glu Val Leu Gly Leu Ile Leu Arg Tyr Val Met Glu Arg Lys Asn Ile Leu Glu Glu Ser Leu Cys Glu Leu Val Ala Lys Gln Leu Lys Gln His Gln Asn Thr Met Glu Asp Lys Phe Ile Val Cys Leu Asn Lys Val Thr Lys Ser Phe Pro Pro Leu Ala Asp Arg Phe Met Asn Ala Val Phe Phe Leu Leu Pro Lys Phe His Gly Val Leu Lys Thr Leu Cys Leu Glu Val Val Leu Cys Arg Val Glu Gly Met Thr Glu Leu Tyr Phe Gln Leu Lys Ser Lys Asp Phe Val Gln Val Met Arg His Arg Asp Glu Arg Gln Lys Val Cys Leu Asp Ile Ile Tyr Lys Met Met Pro Lys Leu Lys Pro Val Glu Leu Arg Glu Leu Leu Asn Pro Val Val Glu Phe Val Ser His Pro Ser Thr Thr Cys Arg Glu Gln Met Tyr Asn Ile Leu Met Trp Ile His Asp Asn Tyr Arg Asp Pro Glu Ser Glu Thr Asp Asn Asp Ser Gln Glu Ile Phe Lys Leu Ala Lys Asp Val Leu Ile Gln Gly Leu Ile Asp Glu Asn Pro Gly Leu Gln Leu Ile Ile Arg Asn Phe Trp Ser His Glu Thr Arg Leu Pro Ser Asn Thr Leu Asp Arg Leu Leu Ala Leu Asn Ser Leu Tyr Ser Pro Lys Ile Glu Val His Phe Leu Ser Leu Ala Thr Asn Phe Leu Leu Glu Met Thr Ser Met Ser Pro Asp Tyr Pro Asn Pro Met Phe Glu His Pro Leu Ser Glu Cys Glu Phe Gln Glu Tyr Thr Ile Asp Ser Asp Trp Arg Phe Arg Ser Thr Val Leu Thr Pro Met Phe Val Glu Thr Gln Ala Ser Gln Gly Thr Leu Gln Thr Arg Thr Gln Glu Gly Ser Leu Ser Ala Arg Trp Pro Val Ala Gly Gln Ile Arg Ala Thr Gln Gln His Asp Phe Thr Leu Thr Gln Thr Ala Asp Gly Arg Ser Ser Phe Asp Trp Leu Thr Gly Ser Ser Thr Asp Pro Leu Val Asp His Thr Ser Pro 

Ser Ser Asp Ser Leu Leu Phe Ala His Lys Arg Ser Glu Arg Leu Gln Arg Ala Pro Leu Lys Ser Val Gly Pro Asp Phe Gly Lys Lys Arg Leu Gly Leu Pro Gly Asp Glu Val Asp Asn Lys Val Lys Gly Ala Ala Gly Arg Thr Asp Leu Leu Arg Leu Arg Arg Arg Phe Met Arg Asp Gln Glu Lys Leu Ser Leu Met Tyr Ala Arg Lys Gly Val Ala Glu Gln Lys Arg Glu Lys Glu Ile Lys Ser Glu Leu Lys Met Lys Gln Asp Ala Gln Val Val Leu Tyr Arg Ser Tyr Arg His Gly Asp Leu Pro Asp Ile Gln Ile Lys His Ser Ser Leu Ile Thr Pro Leu Gln Ala Val Ala Gln Arg Asp Pro Ile Ile Ala Lys Gln Leu Phe Ser Ser Leu Phe Ser Gly Ile Leu Lys Glu Met Asp Lys Phe Lys Thr Leu Ser Glu Lys Asn Asn Ile Thr Gln Lys Leu Leu Gln Asp Phe Asn Arg Phe Leu Asn Thr Thr Phe Ser Phe Phe Pro Pro Phe Val Ser Cys Ile Gln Asp Ile Ser Cys Gln His Ala Ala Leu Leu Ser Leu Asp Pro Ala Ala Val Ser Ala Gly Cys Leu Ala Ser Leu Gln Gln Pro Val Gly Ile Arg Leu Leu Glu Glu Ala Leu Leu Arg Leu Leu Pro Ala Glu Leu Pro Ala Lys Arg Val Arg Gly Lys Ala Arg Leu Pro Pro Asp Val Leu Arg Trp Val Glu Leu Ala Lys Leu Tyr Arg Ser Ile Gly Glu Tyr Asp Val Leu Arg Gly Ile Phe Thr Ser Glu Ile Gly Thr Lys Gln Ile Thr Gln Ser Ala Leu Leu Ala Glu Ala Arg Ser Asp Tyr Ser Glu Ala Ala Lys Gln Tyr Asp Glu Ala Leu Asn Lys Gln Asp Trp Val Asp Gly Glu Pro Thr Glu Ala Glu Lys Asp Phe Trp Glu Leu Ala Ser Leu Asp Cys Tyr Asn His Leu Ala Glu Trp Lys Ser Leu Glu Tyr Cys Ser Thr Ala Ser Ile Asp Ser Glu Asn Pro Pro Asp Leu Asn Lys Ile Trp Ser Glu Pro Phe Tyr Gln Glu Thr Tyr Leu Pro Tyr Met Ile Arg Ser Lys Leu Lys Leu Leu Leu Gln Gly Glu Ala Asp Gln Ser Leu Leu Thr Phe Ile Asp Lys Ala Met His Gly Glu Leu Gln Lys Ala Ile Leu Glu Leu His Tyr Ser Gln Glu Leu Ser Leu Leu Tyr Leu Leu Gln Asp Asp Val Asp Arg Ala Lys Tyr Tyr Ile Gln Asn 

Gly Ile Gln Ser Phe Met Gln Asn Tyr Ser Ser Ile Asp Val Leu Leu His Gln Ser Arg Leu Thr Lys Leu Gln Ser Val Gln Ala Leu Thr Glu Ile Gln Glu Phe Ile Ser Phe Ile Ser Lys Gln Gly Asn Leu Ser Ser Gln Val Pro Leu Lys Arg Leu Leu Asn Thr Trp Thr Asn Arg Tyr Pro Asp Ala Lys Met Asp Pro Met Asn Ile Trp Asp Asp Ile Ile Thr Asn Arg Cys Phe Phe Leu Ser Lys Ile Glu Glu Lys Leu Thr Pro Leu Pro Glu Asp Asn Ser Met Asn Val Asp Gln Asp Gly Asp Pro Ser Asp Arg Met Glu Val Gln Glu Glu Glu Asp Ile Ser Ser Leu Ile Arg Ser Cys Lys Phe Ser Met Lys Met Lys Met Ile Asp Ser Ala Arg Lys Gln Asn Asn Phe Ser Leu Ala Met Lys Leu Leu Lys Glu Leu His Lys Glu Ser Lys Thr Arg Asp Asp Trp Leu Val Ser Trp Val Gln Ser Tyr Cys Arg Leu Ser His Cys Arg Ser Arg Ser Gln Gly Cys Ser Glu Gln Val Leu Thr Val Leu Lys Thr Val Ser Leu Leu Asp Glu Asn Asn Val Ser Ser Tyr Leu Xaa Lys Asn Ile Leu Ala Phe Arg Asp Gln Asn Ile Leu Leu Gly Thr Thr Tyr Arg Ile Ile Ala Asn Ala Leu Ser Ser Glu Pro Ala Cys Leu Ala Glu Ile Glu Glu Asp Lys Ala Arg Arg Ile Leu Glu Leu Ser Gly Ser Ser Ser Glu Asp Ser Glu Lys Val Ile Ala Gly Leu Tyr Gln Arg Ala Phe Gln His Leu Ser Glu Ala Val Gln Ala Ala Glu Glu Glu Ala Gln Pro Pro Ser Trp Ser Cys Gly Pro Ala Ala Gly Val Ile Asp Ala Tyr Met Thr Leu Ala Asp Phe Cys Asp Gln Gln Leu Arg Lys Glu Glu Asn Ala Ser Val Thr Asp Ser Ala Glu Leu Gln Ala Tyr Pro Ala Leu Val Val Glu Lys Met Leu Lys Ala Leu Lys Leu Asn Ser Asn Glu Ala Arg Leu Lys Phe Pro Arg Leu Leu Gln Ile Ile Glu Arg Tyr Pro Glu Glu Thr Leu Ser Leu Met Thr Lys Glu Ile Ser Ser Val Pro Cys Trp Gln Phe Ile Ser Trp Ile Ser His Met Val Ala Leu Leu Asp Lys Asp Gln Ala Val Ala Val Gln His Ser Val Glu Glu Ile Thr Asp Asn Tyr Pro Gln Ala Ile Val Tyr Pro Phe Ile Ile Ser Ser 



Glu Ser Tyr Ser Phe Lys Asp Thr Ser Thr Gly His Lys Asn Lys Glu Phe Val Ala Arg Ile Lys Ser Lys Leu Asp Gln Gly Gly Val Ile Gln Asp Phe Ile Asn Ala Leu Asp Gln Leu Ser Asn Pro Glu Leu Leu Phe Lys Asp Trp Ser Asn Asp Val Arg Ala Glu Leu Ala Lys Thr Pro Val Asn Lys Lys Asn Ile Glu Lys Met Tyr Glu Arg Met Tyr Ala Ala Leu Gly Asp Pro Lys Ala Pro Gly Leu Gly Ala Phe Arg Arg Lys Phe Ile Gln Thr Phe Gly Lys Glu Phe Asp Lys His Phe Gly Lys Gly Gly Ser Lys Leu Leu Arg Met Lys Leu Ser Asp Phe Asn Asp Ile Thr Asn Met Leu Leu Leu Lys Met Asn Lys Asp Ser Lys Pro Pro Gly Asn Leu Lys Glu Cys Ser Pro Trp Met Ser Asp Phe Lys Val Glu Phe Leu Arg Asn Glu Leu Glu Ile Pro Gly Gln Tyr Asp Gly Arg Gly Lys Pro Leu Pro Glu Tyr His Val Arg Ile Ala Gly Phe Asp Glu Arg Val Thr Val Met Ala Ser Leu Arg Arg Pro Lys Arg Ile Ile Ile Arg Gly His Asp Glu Arg Glu His Pro Phe Leu Val Lys Gly Gly Glu Asp Leu Arg Gln Asp Gln Arg Val Glu Gln Leu Phe Gln Val Met Asn Gly Ile Leu Ala Gln Asp Ser Ala Cys Ser Gln Arg Ala Leu Gln Leu Arg Thr Tyr Ser Val Val Pro Met Thr Ser Ser Asp Pro Arg Ala Pro Pro Cys Glu Tyr Lys Asp Trp Leu Thr Lys Met Ser Gly Lys His Asp Val Gly Ala Tyr Met Leu Met Tyr Lys Gly Ala Asn Arg Thr Glu Thr Val Thr Ser Glu Arg Lys Arg Glu Ser Lys Val Pro Ala Asp Leu Leu Lys Arg Ala Phe Val Arg Met Ser Thr Ser Pro Glu Ala Phe Leu Ala Leu Arg Ser His Phe Ala Ser Ser His Ala Leu Ile Cys Ile Ser His Trp Ile Leu Gly Ile Gly Asp Arg His Leu Asn Asn Phe Met Val Ala Met Glu Thr Gly Gly Val Ile Gly Ile Asp Phe Gly His Ala Phe Gly Ser Ala Thr Gln Phe Leu Pro Val Pro Glu Leu Met Pro Phe Arg Leu Thr Arg Gln Phe Ile Asn Leu Met Leu Pro Met Lys Glu Thr Gly Leu Met Tyr Ser Ile Met Val His Ala Leu Arg Ala Phe Arg Ser Asp Pro Gly Leu Leu Thr Asn 



Thr Met Asp Val Phe Val Lys Glu Pro Ser Phe Asp Trp Lys Asn Phe 3975 Glu Gln Lys Met Leu Lys Lys Gly Gly Ser Trp Ile Gln Glu Ile Asn 3990 3995 Val Ala Glu Lys Asn Trp Tyr Pro Arg Gln Lys Ile Cys Tyr Ala Lys 4005 4010 Arg Lys Leu Ala Gly Ala Asn Pro Ala Val Ile Thr Cys Asp Glu Leu 4020 4025 Leu Leu Gly His Glu Lys Ala Pro Ala Phe Arg Asp Tyr Val Ala Val 4035 4040 4045 Ala Arg Gly Ser Lys Asp His Asn Ile Arg Ala Gln Glu Pro Glu Ser 4055 4060 Gly Leu Ser Glu Glu Thr Gln Val Lys Cys Ile Met Asp Gln Ala Thr 4070 4075 Asp Pro Asn Ile Leu Gly Arg Thr Trp Glu Gly Trp Glu Pro Trp Met 4090 <210> 35 <211> 1014 <212> PRT <213> Human <400> 35 Met Ala Glu Ser Ser Asp Lys Leu Tyr Arg Val Glu Tyr Ala Lys Ser Gly Arg Ala Ser Cys Lys Lys Cys Ser Glu Ser Ile Pro Lys Asp Ser 25 Leu Arg Met Ala Ile Met Val Gln Ser Pro Met Phe Asp Gly Lys Val 40 Pro His Trp Tyr His Phe Ser Cys Phe Trp Lys Val Gly His Ser Ile 55 Arg His Pro Asp Val Glu Val Asp Gly Phe Ser Glu Leu Arg Trp Asp 70 Asp Gln Gln Lys Val Lys Lys Thr Ala Glu Ala Gly Gly Val Thr Gly 85 Lys Gly Gln Asp Gly Ile Gly Ser Lys Ala Glu Lys Thr Leu Gly Asp 105 Phe Ala Ala Glu Tyr Ala Lys Ser Asn Arg Ser Thr Cys Lys Gly Cys 120 125 Met Glu Lys Ile Glu Lys Gly Gln Val Arg Leu Ser Lys Lys Met Val 135 140 Asp Pro Glu Lys Pro Gln Leu Gly Met Ile Asp Arg Trp Tyr His Pro 150 155 Gly Cys Phe Val Lys Asn Arg Glu Glu Leu Gly Phe Arg Pro Glu Tyr

Ser Ala Ser Gln Leu Lys Gly Phe Ser Leu Leu Ala Thr Glu Asp Lys
180
185
190
Clarate Ala Thr Glu Asp Lys

Glu Ala Leu Lys Lys Gln Leu Pro Gly Val Lys Ser Glu Gly Lys Arg

225 230 235 240
Gln Asn Asp Leu Ile Trp Asn Ile Lys Asp Glu Leu Lys Lys Val Cys
245 250 255

Ser Thr Asn Asp Leu Lys Glu Leu Leu Ile Phe Asn Lys Gln Gln Val Pro Ser Gly Glu Ser Ala Ile Leu Asp Arg Val Ala Asp Gly Met Val Phe Gly Ala Leu Leu Pro Cys Glu Glu Cys Ser Gly Gln Leu Val Phe Lys Ser Asp Ala Tyr Tyr Cys Thr Gly Asp Val Thr Ala Trp Thr Lys Cys Met Val Lys Thr Gln Thr Pro Asn Arg Lys Glu Trp Val Thr Pro Lys Glu Phe Arg Glu Ile Ser Tyr Leu Lys Lys Leu Lys Val Lys Lys Gln Asp Arg Ile Phe Pro Pro Glu Thr Ser Ala Ser Val Ala Ala Thr Pro Pro Pro Ser Thr Ala Ser Ala Pro Ala Ala Val Asn Ser Ser Ala Ser Ala Asp Lys Pro Leu Ser Asn Met Lys Ile Leu Thr Leu Gly Lys Leu Ser Arg Asn Lys Asp Glu Val Lys Ala Met Ile Glu Lys Leu Gly Gly Lys Leu Thr Gly Thr Ala Asn Lys Ala Ser Leu Cys Ile Ser Thr Lys Lys Glu Val Glu Lys Met Asn Lys Lys Met Glu Glu Val Lys Glu Ala Asn Ile Arg Val Val Ser Glu Asp Phe Leu Gln Asp Val Ser Ala Ser Thr Lys Ser Leu Gln Glu Leu Phe Leu Ala His Ile Leu Ser Pro Trp Gly Ala Glu Val Lys Ala Glu Pro Val Glu Val Val Ala Pro Arg Gly Lys Ser Gly Ala Ala Leu Ser Lys Lys Ser Lys Gly Gln Val Lys Glu Glu Gly Ile Asn Lys Ser Glu Lys Arg Met Lys Leu Thr Leu Lys Gly Gly Ala Ala Val Asp Pro Asp Ser Gly Leu Glu His Ser Ala His Val Leu Glu Lys Gly Gly Lys Val Phe Ser Ala Thr Leu Gly Leu Val Asp Ile Val Lys Gly Thr Asn Ser Tyr Tyr Lys Leu Gln Leu Leu Glu Asp Asp Lys Glu Asn Arg Tyr Trp Ile Phe Arg Ser Trp Gly Arg Val Gly Thr Val Ile Gly Ser Asn Lys Leu Glu Gln Met Pro Ser Lys Glu Asp Ala Ile Glu His Phe Met Lys Leu Tyr Glu Glu Lys Thr Gly Asn Ala Trp His Ser Lys Asn Phe Thr Lys Tyr Pro Lys Lys Phe Tyr Pro Leu Glu Ile Asp Tyr Gly Gln Asp Glu Glu Ala Val Lys Lys Leu Thr Val Asn Pro Gly Thr Lys Ser Lys Leu Pro Lys Pro Val Gln Asp Leu Ile Lys Met Ile Phe Asp Val Glu Ser Met Lys Lys Ala Met Val Glu 



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Tyr Glu Ile Asp Leu Gln Lys Met Pro Leu Gly Lys Leu Ser Lys Arg
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Gln Ile Gln Ala Ala Tyr Ser Ile Leu Ser Glu Val Gln Gln Ala Val
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                                        715
Ser Gln Gly Ser Ser Asp Ser Gln Ile Leu Asp Leu Ser Asn Arg Phe
                725
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Tyr Thr Leu Ile Pro His Asp Phe Gly Met Lys Lys Pro Pro Leu Leu
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Asn Asn Ala Asp Ser Val Gln Ala Lys Val Glu Met Leu Asp Asn Leu
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Leu Asp Ile Glu Val Ala Tyr Ser Leu Leu Arg Gly Gly Ser Asp Asp
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Ile Lys Val Val Asp Arg Asp Ser Glu Glu Ala Glu Ile Ile Arg Lys
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                                   810
Tyr Val Lys Asn Thr His Ala Thr Thr His Asn Ala Tyr Asp Leu Glu
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Val Ile Asp Ile Phe Lys Ile Glu Arg Glu Gly Glu Cys Gln Arg Tyr
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                           840
                                                845
Lys Pro Phe Lys Gln Leu His Asn Arg Arg Leu Leu Trp His Gly Ser
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                                            860
Arg Thr Thr Asn Phe Ala Gly Ile Leu Ser Gln Gly Leu Arg Ile Ala
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Pro Pro Glu Ala Pro Val Thr Gly Tyr Met Phe Gly Lys Gly Ile Tyr
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                                   890
Phe Ala Asp Met Val Ser Lys Ser Ala Asn Tyr Cys His Thr Ser Gln
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Gly Asp Pro Ile Gly Leu Ile Leu Leu Gly Glu Val Ala Leu Gly Asn
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                                                925
Met Tyr Glu Leu Lys His Ala Ser His Ile Ser Lys Leu Pro Lys Gly
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                                            940
Lys His Ser Val Lys Gly Leu Gly Lys Thr Thr Pro Asp Pro Ser Ala
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Asn Ile Ser Leu Asp Gly Val Asp Val Pro Leu Gly Thr Gly Ile Ser
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Ser Gly Val Asn Asp Thr Ser Leu Leu Tyr Asn Glu Tyr Ile Val Tyr
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